4. (Amended) The adenoviral vector of claim 3, wherein the adenoviral vector is lacking all or part of the E1 region.

5. (Amended) The adenoviral vector of claim 4, wherein the adenoviral vector is lacking all or part of the E1a region and/or is lacking all or part of the E1b region.

6. (Amended) The adenoviral vector of claim 3, wherein the adenoviral vector is lacking all or part of the E4 region.

7. (Amended) The adenoviral vector of claim 3, wherein the adenoviral vector is multiply-deficient.

8. (Amended) The adenoviral vector of claim 7, wherein the adenoviral vector is lacking all or part of the E1 region, all or part of the E3 region, and all or part of the E4 region.

9. (Amended) The adenoviral vector of claim 7, wherein the adenoviral vector is lacking all or part of the E1 region, all or part of the E2 region, and all or part of the E3 region.

10. (Amended) The adenoviral vector of claim 9, wherein the adenoviral vector is further lacking all or part of the E4 region.

11. (Amended) The adenoviral vector of claim 8, wherein the adenoviral vector comprises a nucleic acid sequence encoding a cis-acting factor, wherein the cis-acting factor modulates the expression of the nucleic acid sequence encoding PEDF or a therapeutic fragment thereof.

12. (Amended) The adenoviral vector of claim 11, wherein the cis-acting factor is a MAR sequence or a LCR sequence.

13. (Amended) The adenoviral vector of claim 8, wherein the adenoviral vector further comprises a nucleic acid sequence encoding a trans-acting factor, wherein the trans-acting factor modulates the expression of the nucleic acid sequence encoding

PEDF or a therapeutic fragment thereof, and wherein the nucleic acid sequence encoding a trans-acting factor does not encode an adenoviral E4 region gene product.

14. (Amended) The adenoviral vector of claim 13, wherein the trans-acting factor is selected from the group consisting of HSV ICP0, Ad pTP, CMV UL84, VZV-ORF61, PRV-EP0, CMV-E1, CMV-IE2, CMV-IE86, HIV-tat, HTLV-tax, HBV-X, and AAV-Rep 78.

15. (Amended) The adenoviral vector of claim 1, wherein the regulatory sequences comprise a promoter selected from the group consisting of a CMV promoter, an RSV promoter, an adeno-associated virus p5 promoter, a Lap2 promoter, an EF1α promoter, and a β-actin promoter.

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16. (Amended) The adenoviral vector of claim 15, wherein the regulatory sequences comprise an RSV promoter.

17. (Amended) The adenoviral vector of claim 1, wherein the regulatory sequences comprise an inducible promoter.

18. (Amended) The adenoviral vector of claim 1, wherein the adenoviral vector comprises a chimeric coat protein comprising a nonnative amino acid sequence,

wherein the chimeric virus coat protein directs entry into cells of a vector comprising the chimeric virus coat protein that is more efficient than entry into cells of a vector that is identical except for comprising a wild-type virus coat protein rather than the chimeric virus protein, and

wherein the chimeric virus coat protein binds an endogenous binding site present on the cell surface not recognized by a vector comprising a wild-type virus coat protein.

19. (Amended) The adenoviral vector of claim 18, wherein the nonnative amino acid sequence is inserted into or in place of an internal coat protein sequence.

20. (Amended) The adenoviral vector of claim 1, wherein the adenoviral vector comprises a chimeric virus coat protein comprising a nonnative amino acid sequence inserted into or in place of an internal coat protein sequence,

wherein the chimeric virus coat protein efficiently binds to a broader range of eukaryotic cells than a wild-type virus coat protein and wherein the chimeric virus coat protein is not selective for a specific type of eukaryotic cell.

21. (Amended) The adenoviral vector of claim 1 further comprising one or more additional nucleic acid sequences encoding therapeutic substances other than PEDF or a therapeutic fragment thereof.

22. (Amended) The adenoviral vector of claim 21, wherein one or more additional nucleic acid sequences encodes ciliary neurotrophic factor (CNTF).

23. (Amended) The adenoviral vector of claim 21, wherein one or more additional nucleic acid sequences encodes an atonal-associated peptide.

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24. (Amended) The adenoviral vector of claim 21, wherein one or more additional nucleic acid sequences encodes an anti-angiogenic substance.

25. (Amended) The adenoviral vector of claim 24, wherein the anti-angiogenic substance is a soluble receptor specific for an angiogenic factor.

26. (Amended) The adenoviral vector of claim 25, wherein the soluble receptor specific for an angiogenic factor is a soluble VEGF-R1 receptor.

27. (Amended) The viral vector of claim 21, wherein the therapeutic substances other than PEDF or a therapeutic fragment thereof are linked to an endoplasmic reticulum localization signal peptide.

REMARKS

The Present Invention

The present invention is directed to an adenoviral vector comprising a nucleic acid sequence encoding pigment epithelium-derived factor (PEDF) or a therapeutic fragment thereof. The nucleic acid sequence is operably linked to regulatory sequences necessary for expression of PEDF or a therapeutic fragment thereof.